State of California—Health and Human Services Agency
California Department of Public Health

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Recommendations for Influenza Testing and Reporting 2015-2016

The official start of the 2015–16 influenza season is October 4, 2015. This California Department of Public Health guidance for local health jurisdictions (LHJs) summarizes diagnostic testing guidelines and influenza reporting requirements for the 2015–2016 influenza season (October 4, 2015–October 1, 2016).

I. Highlights

- Continue mandatory reporting of laboratory-confirmed influenza in fatal cases age 0–64 years by using CalREDIE or faxing the Severe Influenza Case History Form to **916-440-5984**.

- Continue voluntary reporting of laboratory-confirmed influenza cases age 0–64 years requiring intensive care by using CalREDIE or faxing the Severe Influenza Case History Form to **916-440-5984**.

- Report acute respiratory outbreaks as soon as possible using CalREDIE or faxing the Preliminary Report of Communicable Disease Outbreak Form to **510-620-3425** in the following situations:
    - Outbreaks in institutions (e.g. long term care facilities, prisons, sleepover camps) with at least **one** case of laboratory confirmed influenza in the setting of a cluster (≥2 cases) of ILI within a 72-hour period.
    - Associated with hospitalizations or fatalities.
    - Assessed as having public health importance (e.g., case(s) have recent exposure to swine, recent travel to an area where novel influenza is circulating, or contact with a confirmed case of swine or novel influenza).

- Encourage influenza testing in the following situations listed below. Note that rapid influenza tests may vary in terms of sensitivity and specificity when compared with viral culture or reverse-transcriptase polymerase chain reaction (RT-PCR), with sensitivities ranging from approximately 50-70%. Laboratory testing with RT-PCR is the preferred testing method when there is strong clinical suspicion, even if the rapid test is negative.
    - Hospitalized, intensive care unit (ICU) and/or fatal cases with ILI
    - Acute respiratory outbreaks

- ILI in any person where history of travel or recent close contacts or exposures within 10 days of symptom onset suggests concern for variant or novel influenza infection (e.g., swine (H3N2v or H1N2v) influenza, influenza A/H7N9 or influenza A/H5). For additional information see:
  - http://www.cdc.gov/flu/swineflu/variant.htm
  - http://www.cdc.gov/flu/avianflu/h7n9/case-definitions.htm
  - http://www.cdc.gov/flu/avianflu/h5n1/testing.htm
  - http://www.cdph.ca.gov/HealthInfo/discond/Documents/CDPH_Influenza_H5N1_H7N9_HPAI_%20Quicksheet_final.pdf

  **Influenza-like illness = fever (>100°F or 37.8°C) and cough and/or sore throat, in the absence of a known cause*

- Collect respiratory specimens for confirmation and further subtyping by real-time RT-PCR at a Respiratory Laboratory Network (RLN) public health laboratory or the CDPH Viral and Rickettsial Disease Laboratory (CDPH-VRDL).

- Work with community partners, e.g. hospital clinicians and clinical laboratories, to remind them of the importance of saving specimens so that further subtyping and characterization can be performed at a public health laboratory.

II. Diagnostic testing

- Influenza real-time RT-PCR testing is available at CDPH-VRDL and at 27 RLN laboratories.

- Upper respiratory samples suitable for RT-PCR include: nasopharyngeal (NP) swabs, nasal swabs, throat swabs, nasal aspirate, nasal washes, NP wash, and NP aspirate. For patients hospitalized with pneumonia, specimens from the lower respiratory tract should also be obtained. Lower respiratory tract samples suitable for RT-PCR include: bronchoalveolar lavage, bronchial wash, tracheal aspirate, and lung tissue.

- Swab specimens should be collected using swabs with a synthetic tip (e.g., polyester or Dacron®) and an aluminum or plastic shaft. Swabs with cotton tips and wooden shafts are NOT recommended. Specimens collected with swabs made of calcium alginate are NOT acceptable.

- Place appropriate swab specimen in a standard container with 2–3 ml of viral transport media (VTM).

- Specimens should be collected within the first 24–72 hours of onset of symptoms and no later than 5 days after onset of symptoms. The specimens should be kept refrigerated at 4°C and sent on cold packs if they can be received by the laboratory within 3 days of the date collected. If samples cannot be received by the laboratory within 3 days, they should be frozen at -70°C or below and shipped on dry ice. The CDPH-VRDL is able to receive specimens Monday through Friday.

Recommendations for RLN laboratories

- During the 2015–2016 influenza season, RLN laboratories are advised to continue broadened surveillance testing for all influenza viruses in persons with:
    - ILI, especially for ICU and fatal cases
    - Outbreaks of acute respiratory illness
    - Cases where history of travel or recent close contacts or exposures within 10 days of symptom onset suggests concern for variant or novel influenza infection (e.g., swine (H3N2v or H1N2v) influenza, influenza A/H7N9 or influenza A/H5), as indicated above.
    - CDPH and CDC recommend testing of all hospitalized cases with ILI, as resources permit and at the discretion of the LHJ.

- To detect novel and possible reassorted viruses, it is important that laboratories use a full real-time RT-PCR subtyping panel (Inf A, H1, H3, pdm Inf A, and pdm H1) to determine subtype. Typical Seasonal Influenza testing results are shown below:

	Influenza real-time RT-PCR results for seasonal influenza viruses				
Influenza real-time RT-PCR Targets:	**Inf A**	**H1**	**H3**	**pdm Inf A**	**pdm H1**
A/H1 2009 pdm virus*	POS	NEG	NEG	POS	POS
A/H1 seasonal virus	POS	POS	NEG	NEG	NEG
A/H3 seasonal virus	POS	NEG	POS	NEG	NEG

* Influenza A(H1N1)pdm09 virus

- Specimens with real-time RT-PCR test results that are inconclusive or meet any of the following criteria should be reported and submitted to CDPH-VRDL for further characterization as soon as possible (contact **Hugo Guevara at 510-248-9855**):
    - Unsubtypeable results with cycle threshold (Ct) value for Flu A ≤ 35
    - Inconclusive results for Influenza A(H1N1)pdm09 virus with Flu A Ct ≤ 35
    - Specimens with results suggesting presence of more than one influenza virus (co-infections)
    - Specimens with results suggestive of variant (swine origin) influenza:

	Influenza real-time RT-PCR results suggestive of variant (swine origin) influenza virus				
Influenza real-time RT-PCR Targets:	**Inf A**	**H1**	**H3**	**pdm Inf A**	**pdm H1**
A/H1 variant virus	POS	POS	NEG	POS	NEG
A/H3 variant virus	POS	NEG	POS	POS	NEG

- RLN laboratories should refer to the Influenza Reference Examination Form for instructions on submission of specimens for further characterization at CDPH-VRDL.

- For ILI cases that test Influenza NEGATIVE, VRDL will accept specimens for further non-influenza respiratory virus testing from cases that have severe or fatal respiratory illness or are part of an outbreak. Please use this form: Non-Influenza testing form.

    - Each week please email influenza test results to CDPH at *InfluenzaSurveillance@cdph.ca.gov*. A template worksheet will be distributed to all RLN labs in a separate email prior to the start of the influenza season. If possible, please note if test results originate from outpatient, hospitalized, ICU or fatal cases.

- For fatal cases, refer available autopsy tissues to CDPH-VRDL for further testing and histopathologic analysis at CDC. On a case-by-case basis, refer to CDPH-VRDL specimens for antiviral resistance testing (e.g. a patient on treatment with persistently positive influenza PCR results). For consultation on these cases, please contact **Hugo Guevara at 510-248-9855**.

- Submit samples to CDPH-VRDL for antiviral viral resistance (AVR) surveillance and strain-typing according to the Influenza RightSize Roadmap sample sizes for your laboratory. The sample sizes will be distributed to all RLN labs in a separate email.

- Generally, the CDPH requests the submission of influenza specimens.
    - Submit laboratory detected influenza viruses to CDPH-VRDL as follows:
        - At the beginning of the influenza season*****
        - During the peak of the influenza season
        - At the end of the influenza season

        ****At beginning of the season*:** submit specimens as they are detected in your laboratory, rather than batching specimens
    - Submit original specimens; if virus has been cultured, also submit the cultured virus

Testing performed at CDPH-VRDL

- Testing at CDPH-VRDL will include outpatient ILI specimens submitted by sentinel providers and reference testing as requested by local public health laboratories.

- CDPH-VRDL and CDC will perform surveillance testing for antiviral resistance and strain-typing on the majority of specimens submitted that have been subtyped by RLN laboratories.

- Questions regarding respiratory virus testing at CDPH-VRDL can be directed to **Hugo Guevara** [*Hugo.Guevara@cdph.ca.gov* or 510-307-8565 or 510-248-9855 (cell)].

III. Reporting of severe influenza cases

- During the 2015–2016 influenza seasons, LHJs should continue mandatory reporting of laboratory-confirmed influenza in fatal cases aged 0–64 years.

- Once the resolution status of an influenza death is set as "confirmed" in CalREDIE, it will be included in the state weekly report, and pediatric deaths will be reported as confirmed to CDC.
- If you plan on issuing a press release regarding your jurisdiction's influenza death(s), please ensure the case(s) has been reported to the CDPH influenza staff (i.e., "confirmed" in CalREDIE or paper case report form has been faxed) and also notify the State Press Office (**Office of Public Affairs, 916-440-7259**) prior to the press release.
- The resolution status should be set to "confirmed" in CalREDIE once the death meets the case definition. If fatal cases reported by your county meeting the case definition have a "suspect" status, please confirm them as soon as your investigation permits. This will help us minimize the lag in reporting of fatal cases and allow our official counts in the state weekly report to be consistent with what is also being reported by LHJs.

- LHJs should report fatal and ICU cases of laboratory-confirmed influenza to CDPH using CalREDIE or faxing the Severe Influenza Case History Form to 916-440-5984.

- LHJs are strongly encouraged to continue voluntary reporting of laboratory-confirmed influenza cases aged 0–64 years requiring intensive care.
  - Once the resolution status of an influenza intensive care admission is set as "confirmed" in CalREDIE, it may be included in the state weekly report.

IV. Reporting of non-TB respiratory outbreaks

- CDPH also requests preliminary reporting of any acute respiratory outbreaks using CalREDIE or faxing the Preliminary Report of Communicable Disease Outbreak Form to 510-620-3425 in the following situations:
  - Outbreaks in institutions (e.g. long term care facilities, prisons, sleepover camps) with at least **one** case of laboratory confirmed influenza in the setting of a cluster (≥2 cases) of ILI within a 72-hour period.
    - Even if it is not influenza season, influenza testing should occur when any resident has signs and symptoms that could be due to influenza, and especially when two residents or more develop respiratory illness within 72 hours of each other.
  - Outbreaks in institutions or congregate settings (e.g., schools, day camps) associated with hospitalizations or fatalities. If the setting is a hospice or long-term care facility, the LHJ should use its judgment as to whether the number of hospitalizations and/or fatalities is above baseline for that institution or setting.

  - Outbreaks in an institution, congregate setting or community where there has been recent exposure to swine for at least one case, or contact with a confirmed case of swine influenza (e.g., H3N2v or H1N2v).

  - Outbreaks in a community assessed by the LHJ as having public health importance.

- Laboratory confirmation can include any positive test performed by any clinical, commercial or local public health laboratory, including by positive rapid antigen test, direct fluorescence assay, culture or PCR. As rapid antigen tests may yield a relatively high proportion of false positive results when influenza prevalence is low, it is recommended that a positive rapid antigen test result be followed up with confirmatory testing using one of the other indicated methods. For cases of severe influenza, specimens should be sent for further sub-typing/characterization to the local public health laboratory or CDPH-VRDL, to enable CDPH to closely monitor influenza viruses that may be novel or resistant to antivirals.

- Preliminary outbreak reports may be completed by LHJs in CalREDIE or by submitting the hardcopy Preliminary Report of Communicable Disease Outbreak Form by email to *CDOUTBREAK@cdph.ca.gov* or fax to 510-620-3425.